

1. (Currently Amended) A method for identifying a compound which modulates ~~for use in modulating, for example promoting,~~ the activation or phosphorylation of an AMPK (AMP-activated protein kinase) or AMPK an AMP-activated protein kinase subfamily member in a cell, the method comprising the steps of (1) determining whether a test compound modulates, ~~for example promotes,~~ the protein kinase activity of LKB1 and (2) selecting a compound which modulates, ~~for example promotes,~~ the protein kinase activity of LKB1, wherein the LKB1 is in a preparation with comprising STRAD ~~and/or or~~ MO25 or both.

2. (Original) The method of claim 1 wherein the LKB1, STRAD or MO25 is recombinant and ~~which~~ is expressed from a recombinant nucleic acid.

3. (Original) A purified preparation comprising LKB1, STRAD and recombinant MO25 expressed from a recombinant nucleic acid.

4. (Currently Amended) The preparation of claim ~~4~~ 3 comprising recombinant LKB1 expressed from a recombinant nucleic acid.

5. (Currently Amended) The preparation of claim ~~3~~ or 4 comprising recombinant STRAD expressed from a recombinant nucleic acid.

6. (Original) A cell capable of expressing LKB1, STRAD and overexpressed or recombinant MO25 expressed from a recombinant nucleic acid.

7. (Original) The cell of claim 6 comprising a recombinant nucleic acid encoding MO25.

8. (Currently Amended) The cell of claim ~~6 or~~ 7 comprising a recombinant nucleic acid encoding LKB1.

9. (Currently Amended) The cell of ~~any one of claims 6 to claim~~ 8 comprising a recombinant nucleic acid encoding STRAD.

10. (Original) A cell comprising LKB1, STRAD and overexpressed or recombinant MO25 expressed from a recombinant nucleic acid.

11. (Original) A cell according to claim 10 comprising recombinant LKB1 expressed from a recombinant nucleic acid.

12. (Currently Amended) A cell according to claim 10 ~~or~~ ~~it~~ comprising recombinant STRAD expressed from a recombinant nucleic acid.

13. Canceled

14. (Currently Amended) A method for making a purified preparation comprising LKB1, STRAD and recombinant MO25 expressed from a recombinant nucleic acid ~~according to any one of claims 3 to 5~~ comprising:

selecting a cell according to claim 10 and
~~the step of~~ purifying the preparation from ~~a the~~ cell ~~according to any one of claims 10 to 13.~~

15. Canceled

16. (Currently Amended) The preparation of ~~any one of claims claim 3 to 5 or 15~~ wherein the LKB1:STRAD:MO25 ratios are 1:1:1.

17. Canceled

18. Canceled

19. (Currently Amended) A method for identifying a compound for modulating cellular LKB1 activity, the method comprising the steps of (1) determining whether a test compound modulates the LKB1 protein kinase activity of a preparation ~~or complex as defined in any one of claims according to claim 3 to 5, 15, 16 or 18 or in a cell as defined in any one of claims 6 to 13~~ and (2) selecting a compound which modulates the said LKB1 protein kinase activity.

20. (Currently Amended) The method of ~~claim 1 or claim 19~~ wherein the LKB1 protein kinase activity is measured using an AMPK or an AMPK subfamily member or a fragment ~~either~~ thereof as the substrate.

21. (Currently Amended) A kit of parts comprising the preparation of claim 3 LKB1 ~~or a recombinant polynucleotide encoding LKB1, STRAD or a recombinant polynucleotide encoding STRAD, and MO25 or a recombinant polynucleotide encoding MO25.~~

22. (Currently Amended) A kit of parts according to claim 21 further comprising (1) an AMPK or an AMPK subfamily member, or recombinant polynucleotide encoding AMPK or AMPK subfamily member or a fragment thereof ~~and (2) a kit of parts as defined in claim 21 or a preparation or complex as defined~~

~~in any one of claims 3 to 5, 15, 16 or 18 or a cell as defined in any one of claims 6 to 13.~~

23. (Currently Amended) A method for overexpressing LKB1 comprising the steps of (1) selecting a cell ~~type according to claim 6 in which to overexpress LKB1, comprising the step of determining whether the cell type is one that expresses STRAD and/or MO25 and~~ (2) overexpressing LKB1 in the selected cell ~~type~~.

24. (Currently Amended) A method according to claim 23 further for preparing LKB1 ~~comprising the steps of (1) overexpressing LKB1 in a cell using a method according to claim 23 and (2) preparing LKB1 from the cell.~~

25. (Original) A method for identifying a putative binding partner for MO25 comprising the steps of (1) providing an amino acid sequence of at least the C-terminal three amino acids of a test putative binding partner (2) selecting a putative binding partner having the C-terminal amino acid sequence Trp-Glu/Asp-Phe.

26. (Original) The method of claim 25 further comprising the step of determining that the selected putative binding partner binds to MO25.

27. (Original) A method for identifying a genetic difference associated with PJS (Peutz-Jeghers Syndrome) comprising the steps of (1) investigating the sequence of a gene encoding a MO25 isoform in at least one patient having PJS (2) identifying any difference between the said patient sequence and equivalent sequence from an individual without PJS.

28. (Original) A method for determining whether an individual is susceptible to PJS comprising the steps of determining whether the test individual has a genetic difference identified as associated with PJS by a method according to claim 27.

29. (Currently Amended) A method for identifying a compound which activates an AMPK or an AMPK subfamily member by a similar mechanism to metformin or phenformin or AICA riboside comprising comparing ~~in which~~ the effect of a test compound on the activation of the AMPK or the AMPK subfamily member by a preparation ~~or complex as defined in any one of claims according to claim 3 to 5, 15, 16 or 18 or a cell as defined in any one of claims 6 to 13 is compared with the~~ effect of metformin or phenformin or AICA riboside on the activation of the AMPK or the AMPK subfamily member and selecting the ~~a~~ compound with a similar effect ~~is selected~~.

30. Canceled

31. (Currently Amended) ~~The method of any one of claims 1, 20 or 29,~~ kit of parts of claim 22, ~~or use of claim 30~~ wherein the AMPK subfamily member is or comprises an AMPK α 1 or AMPK α 2 polypeptide.

32. (Currently Amended) ~~The method of any one of claims 1, 20, 29,~~ kit of parts of claim 22 ~~or use of claim 30~~ wherein the AMPK subfamily member is or comprises a NUA1, NUA2, BRSK1, BRSK2, SIK, QIK, QSK, MARK1, MARK2, MARK3, MARK4 or MELK polypeptide.

33. (Currently Amended) A peptide substrate for LKB1 comprising the amino acid sequence SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID

NO:35, SEQ ID NO:37, LSNLYHQGKFLQTFCGSPLY (SEQ ID NO:16), or FGNFYKSGEPLSTWCGSPPY (SEQ ID NO:17), or LSNMMSDGEFLRTSCGSPNY (SEQ ID NO:18), or MASLQVGDSLLETSCGSPHY (SEQ ID NO:19), or FSNEFTVGGKLDTFCGSPPY (SEQ ID NO:20), or AKPKGKNKDYHLQTCCGSLAY (SEQ ID NO:21); or a said amino acid sequence with from one to four substitutions therein at any position other than the underlined residue and/or a conservative substitution at the underlined residue; or at least ten contiguous residues of a said sequence encompassing the underlined residue.

34. (Currently Amended) A peptide substrate for LKB1 according to claim 1 consisting of the amino acid sequence LSNLYHQGKFLQTFCGSPLY (SEQ ID NO:16), or LSNLYHQGKFLQTFCGSPLYRRR (SEQ ID NO:23), or SNLYHQGKFLQTFCGSPLY (SEQ ID NO:24), or SNLYHQGKFLQTFCGSPLYRRR (SEQ ID NO:25), or ~~LSNLYHQGKFLQTFCGSPLY or LSNLYHQGKFLQTFCGSPLYRRR or~~ FGNFYKSGEPLSTWCGSPPY (SEQ ID NO:17), or FGNFYKSGEPLSTWCGSPPYRRR (SEQ ID NO:29), or LSNMMSDGEFLRTSCGSPNY (SEQ ID NO:18), or LSNMMSDGEFLRTSCGSPNYRRR (SEQ ID NO:31), or MASLQVGDSLLETSCGSPHY (SEQ ID NO: 19), or MASLQVGDSLLETSCGSPHYRRR (SEQ ID NO:33), or FSNEFTVGGKLDTFCGSPPY (SEQ ID NO: 20), or FSNEFTVGGKLDTFCGSPPYRRR (SEQ ID NO: 35), or AKPKGKNKDYHLQTCCGSLAY (SEQ ID NO: 21), or AKPKGKNKDYHLQTCCGSLAYRRR (SEQ ID NO: 37) .

35. (Currently Amended) An antibody reactive with a peptide antigen having the amino acid sequence MVAGLTLGKGPESPDGDVS (SEQ ID NO: 38) (residues 1-20 of human BRSK1), LSWGAGLKGQKVATSYESSL (SEQ ID NO: 39) (residues 655-674 of human BRSK2), MEGAAAPVAGDRPDLGLGAPG (SEQ ID NO: 40) (residues 1-21 of human NUA1), TDCQEVATATYRQALRVCSKLT (SEQ ID NO: 41) (residues 653-673 of human NUA2),

MVMADGPRHLQRGPVRVGFYD (SEQ ID NO: 42) (residues 1-21 of human QIK), MVIMSEFSADPAGQGQGGQK (SEQ ID NO: 43) (residues 1-20 of human SIK), GDCEMEDLMPCSLGTFVLVQ (SEQ ID NO: 44) (residues 765-784 of human SIK), TDILLSYKHPEVSFSMEQAGV (SEQ ID NO: 45) (residues 1349-1369 of human QSK), SGTSIAFKNIASKIANELKL (SEQ ID NO: 46) (residues 776-795 of human MARK1), MSSRTVLAPGNDRNSDTHGT (SEQ ID NO: 47) (residues 1-20 of human MARK4), MKDYDELLKYYELHETIGTG (SEQ ID NO: 48) (residues 1-20 of human MELK), CTSPPDSEFLDDHHLTR (SEQ ID NO: 49) (residues 344-358 of rat AMPK α 1), CDPMKRATIKDIRE (SEQ ID NO: 50) (residues 252 to 264 of rat AMPK α 1).

Respectfully submitted,

January 17, 2006
Date

Karla M. Weyand
Karla M. Weyand
Reg. No. 40,223

Rogalskyj & Weyand, LLP
P.O. Box 44
Livonia, New York 14487-0044
Tel: 716-626-5380
Fax: 716-626-5384